Failure of the vaccination campaign against A(H1N1) influenza in pregnant women in France: Results from a national survey.

Beatrice Blondel, Nada Mahjoub, Nicolas Drewniak, Odile Launay, François Goffinet

FAILURE OF THE VACCINATION CAMPAIGN AGAINST A(H1N1) INFLUENZA IN PREGNANT WOMEN IN FRANCE

Results from a national survey

Béatrice BLONDEL[a,b], Nada MAHJOUB[a,b], Nicolas DREWNIAK[a,b], Odile LAUNAY[c,d], François GOFFINET [a,d,e]

[a] INSERM, UMRS 953, Epidemiological Research Unit on Perinatal and Women's and Children's Health, Paris, France

[b] UPMC Univ Paris 06, Paris, France

[c] INSERM, CIC BT505, Assistance Publique-Hôpitaux de Paris, Hôpital Cochin, Centre d'Investigation Clinique de Vaccinologie Cochin Pasteur, Paris, France

[d] Université Paris-Descartes, Paris, France

[e] Maternité Port-Royal, Hôpital Cochin, Assistance Publique-Hôpitaux de Paris, Paris, France

Corresponding author

Béatrice BLONDEL

INSERM U 953, Hôpital Saint Vincent de Paul, 74 avenue Denfert Rochereau, 75014 Paris cedex, France

Telephone: 33 1 42 34 55 85; fax: 33 1 43 26 89 79

beatrice.blondel@inserm.fr

ABSTRACT

Background and objective: Pregnant women were a priority group for vaccination during the 2009 A(H1N1) influenza pandemic. In France, vaccination was organized in ad hoc centers. Women received vouchers by mail and were given a non-adjuvanted vaccine. Our objective was to assess the national vaccination rate among pregnant women and to determine the association of vaccination with maternal characteristics, prenatal care, and pregnancy-related health behaviors.

Method: Data came from a national representative sample of women who gave birth in March 2010 (N=13 453) and were interviewed in the hospital before discharge; they were in the second trimester of pregnancy during the vaccination campaign. Associations between vaccination and socio-demographic and medical characteristics, region of residence, care providers, and preventive behaviors were assessed with bivariable analyses and logistic regression models.

Results: Vaccine coverage was 29.3% (95% CI: 28.6-30.1). The main reason for not being vaccinated was that women did not want this immunization (91%). In adjusted analyses, vaccination was more frequent in women who were older, employed, born in France, with a parity of 1 or 2 and specific favourable health behaviors. The adjusted odds ratio for women with a postgraduate educational level was 4.1 (95% CI: 3.5-4.8) compared to those who did not complete high school. Women with additional risk factors for complications from A(H1N1) infection had a vaccination rate similar to that of other women.

Conclusion: The vaccination campaign resulted in poor vaccination coverage, strong social inequalities, and no special protection for pregnant women at the highest risk of complications. These findings provide essential information for the organization of future vaccination campaigns.

Keywords: A(H1N1) influenza; vaccination; pregnant women; maternal characteristics; health behavior; health services

INTRODUCTION

The consequences of pandemic and seasonal influenza during pregnancy are well known [1]. Particularly serious effects of A(H1N1) influenza on pregnant women and newborns were reported at the very beginning of the pandemic in July 2009 [2] and were subsequently confirmed [3-4].

International organizations [5-6] advised that all pregnant women be vaccinated against the 2009 A(H1N1) flu, regardless of the type of vaccine or the trimester of pregnancy. In France, vaccination was recommended for the entire population and priority vaccination for some groups at high risk, including pregnant women in the second and third trimesters of pregnancy [7]. A non-adjuvanted vaccine (Panenza®) was recommended for this group, based on doubts about potential risks for fetuses, in contrast with most European countries which used adjuvanted vaccines [8]. The non-adjuvanted vaccine did not become available until November 20, 2009, ie, one month after the beginning of the epidemic [9] and the beginning of the vaccination campaign for the general population [10]. Vaccination was free and was performed most often in special ad hoc vaccination sites, such as local gymnasiums. During the 10 days before the non-adjuvanted vaccine became available, all pregnant women received invitations with vouchers by mail, with a list of vaccination centers close to their home.

The French vaccination campaign took place in a generally unfavorable climate, with heated debates about the utility and risks of vaccination. This resulted in low acceptability of the vaccine [11] and only 7.9% of the general population was vaccinated [12].

Our objectives were to estimate the national rate of vaccination against A(H1N1) influenza in pregnant women and to assess whether vaccination uptake was associated with maternal socio-demographic and medical characteristics, prenatal care, and other maternal health-related behaviors. We used the National Perinatal Survey, carried out in March 2010, to study these questions.

METHODS

The National Perinatal Surveys are conducted routinely to monitor perinatal health. They include all births in one week in all maternity units [13]. Women are interviewed between delivery and discharge

about their socio-demographic characteristics, prenatal care and health behavior. Data on health and obstetric care are collected from medical records. In the 2010 survey, women were asked whether they had been vaccinated against A(H1N1) influenza and, if not, why not. The sample included 14,355 women in mainland France and vaccination uptake was known for 13,453 women.

We studied several categories of determinants of vaccination uptake: maternal socio-demographic characteristics, medical characteristics, prenatal care and health behaviors. The medical characteristics included conditions associated with complications during influenza infection (e.g., diabetes mellitus, asthma, respiratory or renal failure, chronic hepatitis B and C infections, and BMI $\geq$30) [14-15]. In addition, we identified women belonging to priority groups for vaccination, independently of pregnancy [7]: those in contact with children (e.g., teachers and daycare personnel) and those in the health-care sector (e.g., doctors, nurses, and nurses' aides).

The prenatal care characteristics were the number of prenatal visits (classified with respect to the minimum number of visits recommended in France according to the duration of pregnancy), the care provider at the beginning of pregnancy (obstetrician/gynecologist, general practitioner, or midwife), and the use of public or private care. We considered that care was mainly in the private sector if the woman delivered in a private maternity unit, because most of those women receive prenatal care from a private obstetrician/gynecologist associated with the unit.

We studied the following health behaviors: consumption of folic acid in periconceptional period, not smoking during the third trimester of pregnancy, and participating in antenatal classes.

We first assessed the vaccination rate and then studied the factors associated with vaccination uptake. Variables were studied using a bivariate and then a logistic regression analysis. The final model included all the variables which were associated with vaccination at the previous step (p value <0.10). Risk factors for complications from flu infection and high-risk occupations were kept in the model, regardless of the association at the previous stage of analysis. SAS 9.2 software was used for the statistical analyses.

RESULTS

Almost all women (99%) were in the second trimester of pregnancy when the non-adjuvanted vaccine became available. The vaccination rate was 29.3% (95% CI: 28.6-30.1). The main reasons that women reported that they were not vaccinated were: not wanting the vaccine (91.2%), not offered a vaccination (5.3%), already had flu symptoms (1.0%), practical reasons (1.6%), and other reasons (0.9%).

The vaccination rate was higher in older women, in those with parity less than 3, and in those without any risk factor for complications from flu infection (Table 1). Married women, those with a higher educational level, born in France, employed during pregnancy, or at high risk of flu exposure or transmission because of their occupation were also vaccinated more frequently. Among healthcare workers, the vaccination rate was 84% among medical doctors, pharmacists, and dentists, 46% among nurses, midwives, and physical therapists, and 24% in women in less skilled occupations. Variations were also found between regions (results not shown).

The vaccination rate was very low for women who had fewer than the minimum number of visits required by French regulations; it was also lower in women who had care provided by GPs and who had prenatal care mainly in the public sector. Vaccination was less frequent among women who did not take folic acid in the periconception period, who smoked during pregnancy and who did not attend antenatal classes.

In the adjusted model, risk factors for complications and number of prenatal visits were not associated with vaccination. The odds ratio for women with a postgraduate educational level was 4.1 (3.5-4.8), compared to those who did not complete high school; the odds ratios were between 0.6 and 0.8 for women under 25 year old compared to older women, for single women compared to married women, and for women who were born abroad compared to native born women. There was lower vaccination coverage in several regions, including Paris and its metropolitan area (data available on request).

DISCUSSION

In 2009, the rate of vaccination against 2009 A(H1N1) influenza among pregnant women in France was quite low. It was higher among women with a high educational level and those with positive health

behavior during pregnancy. Having medical characteristics associated with the risk of severe influenza complications did not influence the vaccination rate.

The principal strength of our study is that it provides data about a representative national sample of women [13] in the second trimester of pregnancy during the vaccination campaign. Very few European countries were able to provide precise population-based estimates of vaccine coverage among pregnant women [8]. Nonetheless, given the number of topics covered by the national perinatal survey, few questions focused on flu prevention, and we did not evaluate women's views about vaccination and barriers to it in great detail. Women were interviewed after birth, about three months after the vaccination campaign. However memory errors were unlikely because going to a vaccination center was the women's decision and was not easily forgotten (travel to an unusual location, long wait times).

The vaccination rate in our study (29.3%) was higher than the estimate by the agency that monitored vaccination coverage (22.7%). The latter was obtained by comparing the number of invitations sent to to the number of women vaccinated in these centers [12]. It is known that some pregnant women who were vaccinated in a center were not recorded in the campaign's monitoring system [10]. Some others may have been vaccinated in the hospital where they had prenatal visits. Moreover, our sample included women in the 2nd trimester during the vaccination campaign, while vouchers were sent to pregnant women in their 2nd and 3rd trimesters; those in their 3rd trimester may have delivered before they were able to be vaccinated or were too tired to travel and stand in line for a vaccination.

Rates of vaccination among pregnant women were higher than 50% in Quebec and Norway, around 50% in Finland and the USA, and around 25% in the UK, while they were much lower in some other countries [8,16-18]. In France the priority given to pregnant women had an effect, for their vaccination rates were clearly higher than those of the general population (7.9%) [12]. Nonetheless, this rate was lower than in many other countries and did not exceed 50% among women who had jobs at high risk of exposure to and transmission of influenza. The rates observed among health care workers were rather low and suggest that these professionals were not always aware of the utility of vaccination [11,19].

Countries made very different choices in implementing their campaign, and these could have had an effect on population adhesion. Pregnant women in Canada were directed mainly to vaccination

centers [17], in Australia to their GPs [20], and in the US to either a doctor's office, clinic or health center [21]. In France, vaccination was organized in ad hoc centers, mainly to avoid wasting vaccine doses and to deal with the lack of storage capacity in doctors' offices [22]. The health insurance fund sent all pregnant women a personal notification. This was possible because pregnant women must be registered to receive reimbursement of prenatal care expenses. In our study, very few women did not receive the invitation. This direct contact gave all women the opportunity to get similar information about the vaccination campaign. Nonetheless, the exclusion of personal health care providers from the vaccination campaign may have been a 'missed opportunity to increase vaccination uptake' [23]; for example French GPs play a key role in vaccination and management of seasonal influenza and had a positive attitude towards A(H1N1) vaccination. The involvement of obstetricians/gynecologists and midwives would have made vaccination easier, as pregnant women have prenatal visits at least once a month [13]. For instance, a program, which actively involved prenatal care providers and maternity units, resulted in a 77% vaccination rate in an American county [24]. The participation of care providers might also have resulted in wider vaccination coverage for the women with additional risk factors for complications, generally known to their doctor.

Preventive behavior, such as not smoking and attending antenatal classes, were strong predictors of vaccination because women take these actions mainly on their own initiative, in the same way as they went for this vaccination. We also found that high educational level was a major factor associated with vaccination among pregnant women [21,25-26]. Material and financial constraints do not appear to have played an important role, as very few women reported that practical reasons explained why they were not vaccinated. The importance of the sociocultural environment may reflect women's ability to analyze the discordant information put forward by the media and public agencies during that period.

The decision to accept A(H1N1) vaccination depended on many factors: the perception of the risk of being infected by this virus, the perception of the consequences of this flu, worries about vaccine safety, and distrust in the vaccine's effectiveness [11,21,26-29]. These perceptions and worries were reinforced among pregnant women because of the potential consequences for the fetus' development in utero. Knowing all of the reasons that women refused vaccination is essential for clarifying complex information, guiding the messages of information campaigns directed at pregnant women, and developing recommendations for healthcare providers. For instance quality websites with validated

and frequently updated information or telephone services specialized in counseling pregnant women [17,28] were especially useful tools for information diffusion in Canada during the pandemic.

CONCLUSION

The campaign to vaccinate pregnant women against pandemic flu did not meet its objective in France. The initiative for vaccinations was left mainly to women and led to low vaccination coverage, strong social differences in uptake and no special protection for women at the highest risk of complications. Confronted with a novel and urgent situation, health authorities had difficulties developing policies quickly based on limited evidence. The evaluation of these policies is thus essential to help plan for future pandemics [22,30-31]. Lessons learned can also be applied to other vaccination policies, such as for the seasonal flu vaccine, which is expected to be recommended for use during pregnancy in France.

Acknowledgements

This survey was funded in part by the Ministry of Health and was coordinated by INSERM unit 953 (Paris, France) and the Maternal and Child Health Services in each French district. The authors thank the heads of the maternity units, the investigators, and all the women who participated in the survey.

References

[1] Rasmussen SA, Jamieson DJ, Bresee JS. Pandemic influenza and pregnant women. Emerg Infect Dis 2008;14:95-100.

[2] Jamieson DJ, Honein MA, Rasmussen SA, Williams JL, Swerdlow DL, Biggerstaff MS et al. H1N1 2009 influenza virus infection during pregnancy in the USA. Lancet 2009;374:451-458.

[3] Newsome K, Williams J, Way S, Honein M, Hill H, Rasmussen S et al. Maternal and infant outcomes among severely ill pregnant women and postpartum women with 2009 pandemic influenza A (H1N1), United States, April 2009-August 2010. MMWR Morb Mortal Wkly Rep 2011;60:1193-1196.

[4] Pierce M, Kurinczuk JJ, Spark P, Brocklehurst P, Knight M. Perinatal outcomes after maternal 2009/H1N1 infection: national cohort study. Br Med J 2011;342:d3214.

[5] WHO. Experts advice WHO on pandemic vaccine policies and strategies. Pandemic (H1N1) 2009 briefing note 14, http://www.who.int/csr/disease/swineflu/notes/briefing_20091030/en/index.html Accessed on 2012, January 18.

[6] ECDC. Use of specific pandemic influenza vaccines during the H1N1 2009 pandemic, ECDC interim guidance, August 2009. Stockholm 2009.

[7] Haut Conseil de la Santé publique. Actualisation de l'avis relatif aux recommandations sur les priorités sanitaires d'utilisation des vaccins pandémiques dirigés contre le virus grippal A(H1N1)v, Oct 2 2009. http://www.hcsp.fr/explore.cgi/avisrapports. Accessed on 2012, January 18.

[8] Luteijn JM, Dolk H, Marnoch GJ. Differences in pandemic influenza vaccination policies for pregnant women in Europe. BMC Public Health 2011;11:819.

[9] Vaux S, Brouard C, Fuhrman C, Turbelin C, Cohen JM, Valette M et al. Dynamique et impact de l'épidémie A(H1N1)2009 en France métropolitaine. BEH 2010;24-26:259-263.

[10] Guthman JP, Bone A, Nicolau J, Lévy-Bruhl D. Insuffisance de la couverture vaccinale grippale a(H1N1) 2009 en population générale et dans les groupes à risque durant la pandémie 2009-2010 en France. BEHWeb 2010; 3 http://www.invs.sante.fr/behweb/2010/03/index.htm. Accessed on 2011, November 16.

[11] Schwarzinger M, Flicoteaux R, Cortaredona S, Obadia Y, Moatti J-P. Low acceptability of A/H1N1 pandemic vaccination in French adult population: did public health policy fuel public dissonance? PLoS One 2010;5:e10199.

[12] Bone A, Guthmann JP, Nicolau J, Lévy-Bruhl D. Population and risk group uptake of H1N1 influenza vaccine in mainland France 2009-2010: results of a national vaccination campaign. Vaccine 2010;28:8157-8161.

[13] Blondel B, Lelong N, Kermarrec M, Goffinet F. Trends in perinatal health in France between 1995 and 2010: Results from the National Perinatal Surveys. J Gyn Obstet Gynecol Biol Reprod 2012;41:e1-e15.

[14] Dubar G, Azria E, Tesniere A, Dupont H, Le Ray C, Baugnon T et al. French experience of 2009 A/H1N1v influenza in pregnant women. PLos One 2010;5:e13112.

[15] Van Kerkhove MD, Vandemaele KA, Shinde V, Jaramillo-Gutierrez G, Koukounari A, Donnelly CA, et al. Risk factors for severe outcomes following 2009 influenza A (H1N1) infection: a global pooled analysis. PloS Med 2011;8:e1001053

[16] Ahluwalia IB, Jamieson DJ, D'Angelo DV, Singleton JA, Santibanez T, Euler G et al. Seasonal influenza and 2009 H1N1 influenza vaccination coverage among pregnant women, 10 states, 2009-10 influenza season. MMWR Morb Mortal Wkly Rep 2010;59:1541-1545.

[17] Fabry P, Gagneur A, Pasquier J-C. Determinants of A(H1N1) vaccination: cross-sectional study in a population of pregnant women in Quebec. Vaccine 2011;29:1824-1829.

[18] Yates L, Pierce M, Stephens S, Mill AC, Spark P, Kurinczuk JJ et al. Influenza A/H1N1v in pregnancy: an investigation of the characteristics and management of affected women and the relationship to pregnancy outcomes for mothers and infants. Health Technol Assess 2010;14:109-182.

[19] Harris KM, Maurer J, Black CL, Euler GL, LeBaron CW, Singleton JA. Interim results: influenza A (H1N1) 2009 monovalent and seasonal influenza vaccination coverage among health-care personnel -United States, August 2009-January 2010. MMWR Morb Mortal Wkly Rep 2010;59:357-362.

[20] White SW, Peterson RW, Quinlivan JA. Pandemic (H1N1) influenza vaccine uptake in pregnant women entering the 2010 influenza season in Western Australia. Med J Aust 2010;193:405-407.

[21] Ding H, Santibanez TA, Jamieson DJ, Weinbaum CM, Euler GL, Grohskopf LA et al. Influenza vaccination coverage among pregnant women-national 2009 H1N1 Flu Survey (NHFS). Am J Obstet Gynecol 2011;204(6 Suppl 1):S96-106.

[22] Hanquet G, Van Damme P, Brasseur D, De Cuyper X, Gregor S, Holmberg M et al. Lessons learnt from pandemic A(H1N1) 2009 influenza vaccination. Highlights of a European workshop in Brussels (22 March 2010). Vaccine 2011;29:370-377.

[23] Schwarzinger M, Verger P, Guerville MA, Aubry C, Rolland S, Obadia Y, Moatti JP. Positive attitudes of French general practitioners towards A/H1N1 influenza-pandemic vaccination: a missed opportunity of increase vaccination uptakes in the general public? Vaccine 2010;28:2743-2748.

[24] Kay MK, Koelemay KG, Sheng Kwan-Gett T, Cadwell BL, Duchin JS. 2009 Pandemic influenza A vaccination of pregnant women--King County, Washington State, 2009-10. Am J Publ Health 2012:102(Suppl 3):S368-S374.

[25] Freund R, Le Ray C, Charlier C, Avenell C, Treluyer JM, Sakalli D et al. Determinants of non vaccination against pandemic H1N1 influenza in pregnant women: a prospective cohort study. Plos One 2011; 6:e20900.

[26] Steelfisher GK, Blendon RJ, Bekheit MM, Mitchell EW, Williams J, Lubell K et al. Novel pandemic A(H1N1) influenza vaccination among pregnant women: motivators and barriers. Am J Obstet Gynecol 2011;204(6 Suppl 1):S116-123.

[27] Tucker Edmonds BM, Coleman J, Armstrong K, Shea JA. Risk perceptions, worry, or distrust: what drives pregnant women's decisions to accept the H1N1 vaccine? Matern Child Health J 2011;15:1203-1209.

[28] Sakaguchi S, Weitzner B, Carey N, Bozzo P, Mirdamadi K, Samuel N et al. Pregnant women's perception of risk with use of the H1N1 vaccine. J Obstet Gynaecol Can 2011;33:460-467.

[29] Sim JA, Ulanika AA, Katikireddi SV, Gorman D. 'Out of two bad choices, I took the slightly better one': vaccination dilemmas for Scottish and Polish migrant women during the H1N1 influenza pandemic. Public Health 2011;125:505-511.

[30] Greco D, Stern EK, Marks G. Review of ECDC's response to the influenza pandemic 2009-10. Stockholm: ECDC, 2011.

[31] Kendal AP, MacDonald NE. Influenza pandemic planning and performance in Canada 2009. Can J Public Health 2010;101:447-453.

293 **Table I. Vaccination rates and Odds Ratios adjusted for all variables in the table**

	n	Rate %	p	Adjusted OR (1)	95% CI	p
Age (years)			<0.0001			<0.0001
<24	2229	13.0		0.72	0.61-0.84	
25-29	4441	26.7		1		
30-34	4124	36.7		1.29	1.16-1.43	
35 +	2529	36.5		1.50	1.32-1.70	
Parity			<0.0001			<0.0001
0	5916	28.7		1		
1-2	6425	31.4		1.26	1.13-1.40	
3+	995	19.1		1.07	0.86-1.33	
Risk factors for complications			<0.0001			0.4291
No	11866	30.1		1		
Yes	1587	23.3		0.94	0.82-1.08	
Family situation			<0.0001			0.0001
Married & cohabiting with partner	6232	33.1		1		
Cohabiting	6196	28.3		0.88	0.80-0.96	
Not cohabiting	958	12.6		0.64	0.50-0.80	
Educational level			<0.0001			<0.0001
Middle school or less	3720	14.7		1		
High school	2681	19.0		1.06	0.91-1.23	
Some college	2875	30.7		1.56	1.36-1.80	
College	2368	42.2		2.33	2.00-2.70	
Postgraduate	1750	57.0		4.08	3.46-4.81	
Maternal country of birth			<0.0001			
France	11.043	31.8		1		<0.0001
Outside of France	2397	18.0		0.61	0.53-0.70	
Employment during pregnancy			<0.0001			0.0319
No	3885	17.3		0.88	0.78-0.99	
Yes	9448	34.4		1		
Occupation characteristics			<0.0001			0.003
Contact with children	774	51.0		1.26	1.06-1.49	
Healthcare worker	818	39.5		1.23	1.04-1.45	
Other (2)	11861	27.2		1		
Number of visits			<0.0001			0.2712
<Minimum(3)	466	14.8		0.73	0.52-1.01	
Minimum or +1	2288	27.8		1		
Minimum +2 or +3	4450	30.9		0.98	0.86-1.12	
Minimum +4 or more	6037	30.3		0.96	0.85-1.09	
Place of care			<0.0001			0.0015
Mainly public	9696	27.3		1		
Mainly private	3757	34.5		1.17	1.06-1.28	
Main healthcare provider						<0.0001
Ob-gyn	9574	32.4	<0.0001	1		
General practitioner	2904	21.4		0.78	0.69-0.88	
Other	697	21.4		0.82	0.66-1.02	

294
295

Table I (continued)**. Odds Ratios for vaccination adjusted for all variables in the table**

	n	Rate %	p	Adjusted OR (1)	95% CI	p
Folic acid consumption			<0.0001			<0.0001
No	9246	25.6		0.70	0.63-0.77	
Yes	3286	41.8		1		
Smoking during pregnancy			<0.0001			0.0476
No	11042	31.3		1		
Yes	2387	19.9		0.88	0.77-1.00	
Prenatal classes			<0.0001			<0.0001
No	6941	21.4		0.68	0.62-0.76	
Yes	6473	37.9		1		

(1) adjusted for all variables in the table and region (p<0.001), N=11,685

(2) other occupation or no occupation during pregnancy

(3) 7 visits for a full term pregnancy according to French regulation